

***Remarks***

Reconsideration of this Application is respectfully requested.

Claims 36, 37, 40, 41, 43, 44, 46-49, 58, and 59 are pending in the application, with claim 36 being the sole independent claim. Based on the following remarks, Applicants respectfully request that the Examiner reconsider the outstanding rejections and objections and that they be withdrawn.

Applicants thank the Examiner for the careful consideration of Applicants remarks in the Appeal Brief dated August 30, 2006. The Applicants acknowledge the Examiner's withdrawal of the rejections under 35 U.S.C. 112 and 35 U.S.C. 103 over a combination of Brown *et al.* and Ciosk *et al.*

***Description of the Invention***

The present invention is drawn to a method of identifying compounds that have the ability to inhibit sister chromatid separation in eukaryotic cells. This method comprises incubating a test compound together with a separin and a separin substrate and subsequently determining the effect of the test compound on the proteolytic activity of the separin. The separin substrate is a polypeptide comprising the amino acid sequence EXXR, wherein X can be any amino acid.

***Rejections under 35 U.S.C. § 103***

In the Office Action at page 2, the Examiner rejects claims 36, 37, 40, 41, 43, 44, 46-49, and 58 under 35 U.S.C. 103(a) as being unpatentable over Brown *et al.* (Analytic Biochem. 217(1):139-147, 1994, hereinafter "Brown") in view of Nagase *et al.* (DNA

Res. 3(1):17-24, 1996, hereinafter "Nagase") and Nomura *et al.* (DNA Res. 1(5):223-229, 1994, hereinafter "Nomura"). Applicants respectfully traverse this rejection.

Brown discloses a high-throughput fluorometric process for measuring protease activity comprising contacting a peptide with a protease in the presence of an inhibitor test compound. The peptide is a fluorogenic peptide labeled at one end with a UV/blue fluorophore and at the other end a quencher. As the Examiner notes, Brown does not teach incubating a separin and a separin substrate in the presence of a test compound.

Nagase teaches the cDNA KIAA0165, disclosed in the Applicants specification to encode the human separin. Nomura teaches the cDNA KIAA0078, disclosed in the Applicants specification to encode the human SCC1. Neither Nagase nor Nomura indicates a function for the cDNAs described therein.

The Examiner asserts that:

[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the process of Brown et al. such that the human separin taught by Nagase et al. and the human SCC1 taught by Nomura et al. is used in the process taught by Brown et al.... One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of having a fast and simple process for identifying human separin inhibitors, which can be used as anti-cancer agents that inhibit sister chromatid separation in cancer cells.

(*Id.* at page 3)

In order to establish a *prima facie* case of obviousness, it must be shown that the claimed invention *as a whole* would have been obvious from the disclosures and teachings of the prior art. "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." See *In re Spormann*, 53 CCPA 1375, 363 F.2d 444, 150 USPQ 449 (1966).

A *prima facie* case of obviousness has not been established. In order to practice the method of Brown, the skilled artisan must have knowledge of a protease and its substrate. Brown states,

Although used here specifically for the enzyme which cleaves at the amino terminus (N-terminus) of  $\beta$ -amyloid peptide (BAP), this type of radiolabeled substrate is readily applied to the analysis and detection of other endoprotease activities. This method relies on a peptide substrate which contains: (a) the amino acids flanking the enzymatic cleavage site . . .

(*Id.* at p. 139)

The Examiner relies on the disclosures of Nomura and Nagase as allegedly teaching human separin and the human separin substrate. Before Applicants' disclosure of the present invention, it was *not known* that separin was a protease, and it was *not known* that SCC1 was a separin substrate. Without that knowledge, no reason existed at the time of the invention to combine the teachings of Brown with the teachings of Nagase and Nomura. There is nothing in Nagase to suggest that the KIAA0165 protein is a protease. Nagase does not disclose any structural motifs in the KIAA1065 protein, perform any experimentation that would suggest a function for the KIAA1065 protein, or even hypothesize a role for the KIAA1065 protein. At most, Nagase reveals that the KIAA0165 protein has a weak similarity to the *S. pombe* cut1 protein. Likewise, there is nothing in Nomura to suggest that the KIAA0078 protein is a protease substrate. Nomura reveals only that the KIAA0078 protein has a weak similarity to the *S. pombe* rad21 protein.

In fact, the references cited by the Examiner that reveal separin to be a protease and Scc1 to be its substrate (Waizenegger *et al.*, Sumara *et al.*, and Hauf *et al.*) were published by the Applicants research group *after* the filing date of the present

application. These discoveries form the basis of the present invention. The reasoning behind the obviousness rejection constitutes impermissible hindsight. It is well established that the reason to combine references, as evidence of obviousness, must come from the prior art. "The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." (See MPEP 2143; *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, Fed. Cir. 1991.) "[I]t is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious. . . . This court has previously stated that '[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.' " (*In re Fritch*, 972 F.2d 1260, 23 USPQ2d 1780, Fed. Cir. 1992.) Without Applicant's specification, what would lead one of ordinary skill in the art to select, out of the myriad of known cDNA sequences and the amino acid sequences encoded thereby, separin and SCC1?

The rejection is not supported by any evidence or explanation as to why a person of ordinary skill in the art, at the time of the invention, would have reason to believe that the KIAA0165 protein is a protease and that the KIAA0078 protein is the substrate of the KIAA0165 protein. Without such knowledge, one of ordinary skill in the art would not have had any reason to conduct an assay employing separin as a protease and SCC1, or a fragment thereof, as a substrate. To combine references without evidentiary support, at least some suggestion or reason found within the prior art, constitutes impermissible hindsight.

The Applicants note the Examiner's comment that "[n]o patentable weight is given to the preamble of these process claims since it merely recites the purpose of these process claims." (*Id.* at page 3.) Consideration or lack thereof given to the preamble is not relevant, as the body of the claim contains a limitation to the use of a separin and a separin substrate.

Therefore, Applicants respectfully submit that the Examiner has not met the burden of establishing a *prima facie* case of obviousness, as no evidence of a reason to combine the teachings of Nagase and Nomura with those of Brown has been presented. In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a).

***Objection to Claim 59***

The Applicants acknowledge the Examiner's objection to claim 59 as being dependent upon a rejected base claim. The Applicants gratefully note the Examiner's finding that claim 59 would be allowable if rewritten in independent form.

***Conclusion***

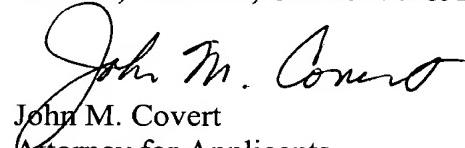
All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will

expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

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